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ABSTRACT

This fact sheet uses a question-and-answer format to summarize what is known about phenylketonuria (PKU), an inherited metabolic disease that leads to mental retardation and other developmental disabilities if untreated in infancy. Questions and answers address the following topics: what PKU is; how PKU is inherited; the diagnosis of PKU; the accuracy of PKU testing and guidelines for testing; the treatment of PKU; the current recommendation that those affected by PKU remain on a restricted diet indefinitely; the associated risks that pregnant PKU mothers face; and screening for other metabolic disorders associated with mental retardation. (DB)

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Phenylketonuria (PKU)

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The Arc
A national organization on mental retardation

S. A. Davis

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Q&A

Phenylketonuria (PKU)

What is PKU?

PKU, which stands for Phenylketonuria, is an inherited metabolic disease (also called an inborn error of metabolism) that leads to mental retardation and other developmental disabilities if untreated in infancy. With an inborn error of metabolism, the body is unable to produce proteins or enzymes needed to convert certain toxic chemicals into nontoxic products, or to transport substances from one place to another (Glanze, 1996).

The body's inability to carry out these vital internal functions may result in neurological damage. In the case of PKU, the amino acid called phenylalanine accumulates. As phenylalanine builds up in the bloodstream, it causes brain damage. Infants with untreated PKU appear to develop typically for the first few months of life, but by twelve months of age most babies will have a significant developmental delay and will be diagnosed with mental retardation before school entry.

How is PKU inherited?

PKU is inherited as a single-gene disorder. Single-gene disorders are caused by a mutant or abnormal gene. They can be inherited in one of three patterns: autosomal dominant, autosomal recessive and X-linked. PKU is an autosomal recessive disorder. Each parent of a child with PKU carries one defective gene for the disorder and one normal gene. In a recessive condition, an individual must have two defective genes in order to have the disorder. Individuals with only one copy of a defective gene are called "carriers," show no symptoms of having the disease, and usually remain unaware of their status until they have an affected child. In order for a child to inherit PKU, both parents must be PKU carriers. When this occurs, there is a one in four chance of their producing an affected child with each pregnancy. Boys and girls are equally at risk of inheriting this disorder.

How is PKU diagnosed?

Before the 1960s, most infants born with PKU developed mental retardation and cerebral palsy. Although treatment for PKU using a low phenylalanine diet was first described in the 1950s, the inability to detect PKU early in the child's life limited effective treatment.

The first newborn screening test was developed by Dr. Robert Guthrie in 1959 specifically to test for PKU. This simple, yet very effective and economical test was developed to screen newborn infants for PKU before leaving the hospital. Today, all states routinely screen newborns for PKU. To test for PKU, the infant's heal is pricked and a few drops of blood are taken. This blood sample is then tested in a state laboratory for abnormal amounts of phenylalanine.

The normal phenylalanine level is less than 2 mg/dl. Those with phenylalanine levels of 20.0 milligrams per deciliter (mg/dl) or higher are considered likely to have "classical" PKU (Yanicelli, Davidson & vanDoornick, 1986). Infants with these high levels are further tested to confirm the diagnosis before treatment is started. Some infants will have more modest elevations of blood phenylalanine and are said to have "mild hyperphenylalanemia." Today many clinicians believe that any child with a phenylalanine level greater than 6 or 8 mg/dl should be treated with a modified phenylalanine restricted diet.

Is testing for PKU 100 percent accurate?

Experts recommend that testing for PKU should be done when the infant is at least twenty-four hours of age but less than seven days old. If an infant is tested too soon after birth, there is a chance that some cases of PKU will be missed as the phenylalanine level will not

QUICK FACTS

Condition: *Phenylketonuria (PKU)*

Link to mental retardation: *Brain damage leading to mental retardation that occurs in children with PKU due to high blood levels of phenylalanine that is not properly metabolized (broken down).*

Primarily affects: *Newborns; more common among North European descent, less common among Jewish, Asian and African-American families.*

Symptoms: *Typical appearance during first few months after birth, but at three - five months will lose interest in surroundings and have mental retardation by twelve months old. Often irritable, restless, destructive. May have dry skin or rashes, a strong, musty body odor and convulsions.*

Incidence: *One in every 12,000 to 15,000 babies is born with PKU in the U.S.*

Cause: *An inherited disorder caused by a build up of an amino acid called phenylalanine that, if left untreated, causes mental retardation. The higher the level of phenylalanine within the body, generally the more severe the disability.*

Treatment: *A low-protein diet consisting of foods that have little or no phenylalanine can decrease the high levels of phenylalanine and prevent the occurrence of mental retardation. All babies in the U.S. are routinely screened for PKU.*

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have risen yet. Now that many hospitals are discharging mothers and infants twenty-four hours after birth, there is a greater likelihood of this happening. The American Academy of Pediatrics recommends that infants receiving the test during the first twenty-four hours of life be re-tested at two to three weeks of age during their first postnatal pediatric visit (March of Dimes, 1994).

How is PKU treated?

Although PKU is not preventable, its symptoms can often be treated successfully through the use of a carefully regimented diet. The diet consists of foods that have a restricted phenylalanine content. Babies are given a special formula that contains very low phenylalanine levels; then they gradually progress to eating certain vegetables and other foods that are low in phenylalanine. Affected children must have their blood tested regularly to ensure the presence of the correct level of phenylalanine.

Foods recommended for those affected by PKU contain small amounts of protein, such as fruits and vegetables, limited amounts of cereal and grain products and special low protein products available through mail-order. High protein foods such as meat, fish, eggs, poultry, dairy products, nuts, peanut butter, legumes, soy products and products containing Nutrasweet should be avoided (Yannicelli, Davidson & vanDoornick, 1986).

The food program used to treat those with PKU is quite expensive, typically costing up to $10,000 a year or more. Although health departments may pay for the formula in some states and mandated insurance coverage may cover the cost in other states, most insurance companies do not cover the cost of treatment for children/adults with PKU because it is considered nutritional rather than medical therapy.

While phenylalanine restricted diets have proven to be highly effective in preventing mental retardation, it is now recognized that there may still be subtle cognitive deficits. Usually the individual has a normal IQ, but the incidence of attention deficit hyperactivity disorder (ADHD) and learning disabilities is higher compared to those children who do not have PKU (Yanicelli, Davidson & vanDoornick, 1986).

Do those affected by PKU have to stay on a regimented diet all their lives?

It was believed in the past that children could discontinue the diet when they turned five to six years old. Recent studies have found that children with PKU who did stop the diet in early childhood did not develop as rapidly as children who remained on the diet, and had more learning disabilities, behavioral problems, and other neurological problems. Thus, until research provides alternative treatments, all persons with PKU should remain on a restricted diet indefinitely in order to maintain a safe level of phenylalanine (believed to be in the range of 2-6 mg/dl) (Schuett, 1996).

What happens when women with PKU have children?

When women with PKU who are not receiving dietary therapy become pregnant, their high levels of phenylalanine can damage their unborn child, causing mental retardation and other congenital defects. High levels of phenylalanine are extremely toxic to the brain of a fetus. Thus, although the child does not have PKU, he or she will have sustained brain damage from the toxic effects of phenylalanine in utero (in the womb). This is known as **MATERNAL PKU**.

More than 90 percent of infants born to women with PKU who are not on a specialized diet will have mental retardation, and may also have small head size (microcephaly), heart defects and low birth weight. These infants cannot be treated with a special diet since they do not have PKU. Therefore, women who have PKU should be on a phenylalanine restricted diet at least one year before pregnancy and should stay on the diet while breast-feeding to increase the chance of having a healthy child (Levy, 1988).

Are other rare metabolic disorders associated with mental retardation being screened for as well as PKU?

Dr. Guthrie's newborn screening test for PKU sparked the testing for other rare metabolic disorders associated with mental retardation: congenital hypothyroidism, galactosemia, homocystinuria, biotinidase deficiency and maple syrup urine disease. While all states and the District of Columbia screen for PKU, only some states screen for the other metabolic conditions (The Arc, 1994).

The development of a screening test for PKU was a significant step toward preventing mental retardation caused by metabolic disorders. Unfortunately, there remain more than 100 rare metabolic disorders that lead to mental retardation for which newborn screening is currently unavailable (McKusick, 1994).

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